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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
KRUSE, DAVID H	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 02/17/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,885	MISRA ET AL.	
	Examiner	Art Unit	
	David H Kruse	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 November 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *10,11,13 and 15* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,12,14 and 16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a)☐ The translation of the foreign language provisional application has been received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9/01* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group 1, claims 1-9, 11, 12, and 14, in the response filed 18 November 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 10, 11, 13 and 15 are withdrawn from further consideration pursuant to 37 CFR § 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the response filed 18 November 2003.

3. This application contains claims 10, 11, 13 and 15 drawn to an invention nonelected with traverse in the response filed 18 November 2003. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR § 1.144) See MPEP § 821.01.

4. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR § 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR § 1.48(b) and by the fee required under 37 CFR § 1.17(i).

Information Disclosure Statement

5. The information disclosure statement filed 17 September 2001 has been considered, a signed copy is attached hereto.

Specification

6. The drawings are acceptable to the Examiner.

7. The abstract of the disclosure does not commence on a separate sheet in accordance with 37 CFR § 1.52(b)(4). A new abstract of the disclosure is required and must be presented on a separate sheet, apart from any other text.

8. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code at page 13, lines 8 and 10. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

9. The disclosure is objected to because of the following informalities: At page 29, line 1, "C ntaining" appears to be a typographical error. Appropriate correction is required.

Sequence Rules

10. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR § 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR §§1.821 through 1.825. Specifically, page 3, lines 24 and 25; page 4, line 27; page 18, line 8; page 26, line 26; page 27, line 30; page 29, line 22of the Specification disclose amino acid sequences of 4 or more residues. Applicant must submit a CRF copy and

paper copy of the Sequence Listing, a statement that the content of the paper and computer readable copies are the same and where applicable include no new matter as required by 37 C.F.R. §§ 1.821(e) or 1.821(f) or 1.821(g) or 1.825(d), as well as an amendment directing its entry into the specification or other appropriate action. Failure to take corrective action will be considered non-responsive to this Office action.

Claim Objections

11. Claim 14 is objected to for being dependent upon a withdrawn claim. For the purposes of this Office action, all of the limitations of claim 13 will be read into claim 14. Appropriate correction is required.

12. Claims 3-5 and 9 are objected to because "A transgenic plant" should read -- The transgenic plant -- in referring to a previous claim.

Claim Rejections - 35 USC § 112

13. The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

14. Claims 1-9, 19 and 20 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The instant claims are indefinite because the limitation "a dermaseptin cationic peptide" does not teach the metes and bounds of the claimed invention. Applicant's teachings on pages 3 of the specification render the claims unclear because the art recognizes "dermaseptin" to mean a cationic, antibiotic peptide isolated from a species of the genus *Phyllomedusa* (Brazilian tree frogs).

15. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

16. Claims 1-9, 19 and 20 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant claims a transgenic plant expressing a dermaseptin cationic peptide and a method of making same.

Applicant describes transgenic plants and methods of making, comprising a nucleic acid encoding dermaseptin peptides having the amino acid sequence of SEQ ID NO: 3 or 28 (dermaseptin b and dermaseptin B, respectively).

Applicant does not describe transgenic plants comprising a nucleic acid encoding other dermaseptin peptides or dermaseptin peptides having one or more conservative amino acid substitutions or at least 40% sequence identity to SEQ ID NO: 3 having dermaseptin biological activity.

Hence, it is unclear from the instant specification that Applicant was in possession of the invention as broadly claimed.

See *University of California V. Eli Lilly and Co.*, 43 USPQ2d 1398 (Fed. Cir. 1997), which teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an

adequate written description of the actual cDNA from that organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism. At 1406, the court states that a description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. In the instant case, the claims read on transgenic plants comprising nucleic acid molecules encoding dermaseptins isolated from other species of the genus *Phyllomedusa* and modifications thereof.

See also, MPEP § 2163 which states that the claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. In the instant case the claimed invention is described only by function "has dermaseptin biological activity" wherein the functional characteristics do not describe the structure. Cationic peptide antibiotics are a diverse genus of which dermaseptin is only a small subspecies (see Hancock and Chapple 1999, Antimicrobial Agents and Chemotherapy 43(6): 1317-1323, especially page 1317, right column).

17. Claims 1-9, 19 and 20 rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for transgenic plants comprising a nucleic acid encoding the amino acid sequence of SEQ ID NO: 3 (dermaseptin b) or SEQ ID NO: 28 (dermaseptin B), does not reasonably provide enablement for transgenic plants comprising a nucleic acid encoding any peptide having dermaseptin biological activity or structural modifications thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Applicant claims a transgenic plant expressing a dermaseptin cationic peptide and a method of making same.

Applicant teaches transgenic plants and methods of making, comprising a nucleic acid encoding dermaseptin peptides having the amino acid sequence of SEQ ID NO: 3 or 28 (dermaseptin b and dermaseptin B, respectively).

Applicant does not teach transgenic plants comprising a nucleic acid encoding other dermaseptin peptides or dermaseptin peptides having one or more conservative amino acid substitutions or at least 40% sequence identity to SEQ ID NO: 3 having dermaseptin biological activity.

In re Wands, 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988) lists eight considerations for determining whether or not undue experimentation would be necessary to practice an invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art,

the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Applicant provides limited guidance on how to make and use transgenic plants expressing a dermaseptin cationic peptide as broadly claimed. The art teaches that the specific function of dermaseptins varies by structure and that the selectivity of these peptides vary (Wechselberger 1998, Biochemica et Biophysica Acta 1388:279-283, see page 282). Expression of cecropin B, a cationic peptide with antimicrobial activity, in a plant was found to be unpredictable because it appeared that the expressed peptide was degraded within seconds in plant cell extracts and did not lead to the predicted resistance (see Florack *et al* 1995, Transgenic Research 4:132-141, see page 132). Even when peptides are not degraded in the transgenic plants, they unexpectedly do not retain their biological activity. Peptides that are effective pesticides when isolated and contacted with microorganisms or fed to insects do not function as pesticides when genes encoding them are transformed into plants. When tobacco plants were transformed with a gene encoding cecropin B, the transformed plants displayed no increase in disease resistance (Hightower et al, 1994, Plant Cell Rep. 13:295-299, see pg 297, paragraph spanning the columns, to pg 298, right column, paragraph 1). De Bolle et al (1996, Plant Mol. Biol. 31:993-1008) teach that tobacco plants transformed with genes encoding seed antimicrobial peptides had no increase in resistance to infection (pg 1004, paragraph spanning the columns). Lastly, Pang et al (1992, Gene 116:165-172) teach that in tobacco plants transformed with a gene encoding the scorpion insectotoxin I_5A, the peptide is not correctly processed and the

resulting plants had no paralytic effect on tobacco budworm (pg 170, right column). Hence, given Applicant's limited guidance, the nature of the invention and the unpredictability of expressing antimicrobial cationic peptides in plant, it would have required undue trial and error experimentation by one of skill in the art at the time of Applicant's invention to make and use transgenic plants expressing a dermaseptin cationic peptide as broadly claimed, especially given Applicant's teachings of what is encompassed by "a dermaseptin cationic peptide" on page 3 of the instant specification.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. Claims 1-6, 8, 9, 12, 14 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Scheffler *et al* (EP 0 552 559 A2, published 28 July 1993) in view of Strahilevitz *et al* (1994, Biochemistry 33: 10951-10960) and in further view of Steinberg *et al* (US Patent 6,025,326, filed 21 November 1996).

Scheffler *et al* teach transgenic plants comprising a nucleic acid encoding a magainin peptide of the South African clawed frog that has antimicrobial activity and a method of making such transgenic plants (see pages 6 and 7).

Scheffler *et al* do not teach transgenic plants comprising a nucleic acid encoding a dermaseptin cationic peptide.

Strahilevitz *et al* teach nucleic acids encoding dermaseptin b and dermaseptin B (which comprises the N-terminal peptide sequence AMWK) (see Figure 7 on page 10959, for example).

Steinberg *et al* teach that it is desirable to transform plants with gene encoding dermaseptin antimicrobial peptides (see column 6, last paragraph and column 19, 3rd and 4th paragraphs).

Hence, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of Applicant's invention to modify the teachings of Scheffler *et al* to substitute the nucleic acid encoding a magainin peptide for a nucleic acid encoding either dermaseptin b or dermaseptin B as taught by Strahilevitz *et al*. Steinberg *et al* motivates one of ordinary skill in the art to make transgenic plants comprising nucleic acids encoding dermaseptin cationic peptides, and given the success of Scheffler *et al* in expressing magainin peptide encoding nucleic acids in plants, one of ordinary skill in the art would have had a reasonable expectation of success in expressing a dermaseptin cationic peptide in a plant as claimed by Applicant. In addition, Strahilevitz *et al* teach that dermaseptin B, which comprises the N-terminal peptide extension AMWK has higher antimicrobial activity than dermaseptin b without the extension, thus one of ordinary skill in the art would have been motivated to express dermaseptin B preferentially in a transgenic plant.

Conclusion

20. Claim 7 is free of the prior art which neither teaches nor suggest a transgenic plant comprising a recombinant nucleic acid molecule encoding a fusion peptide having the formula P-S-D as claimed.

21. No claims are allowed.

22. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David H. Kruse, Ph.D. whose telephone number is (571) 272-0799. The examiner can normally be reached on Monday to Friday from 8:00 a.m. to 4:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Amy Nelson can be reached at (571) 272-0804. The fax telephone number for this Group is (703) 872-9306 Before Final or (703) 872-9307 After Final.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group Receptionist whose telephone number is (703) 308-0196.

David H. Kruse
AU 1638

David H. Kruse, Ph.D.
9 February 2004